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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/541,094	03/31/00	ST. GEORGE-HYSLOP	P 1034/1F812-U

EXAMINER	
BRUNOVSKIS, P	
ART UNIT	**PAPER NUMBER**
1632	11

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DATE MAILED: 08/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev. 2/95)

*U.S. GPO: 2000-473-000/44602

Office Action Summary	Application No. 09/541,094	Applicant(s) ST. GEORGE-HYSLOP ET AL.	
	Examiner Peter Brunovskis	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-6,9,18-28 and 30-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10-17 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group II, claims 7-17 and 29 and of the species directed to human PAMP polynucleotide sequence of SEQ ID in Paper No. 10, filed 6/20/01 is acknowledged. The traversal is on the ground(s) that Groups I-VI fail to define inventions that warrant separate examination and search because the claims of all groups are unified by the same novel feature, namely PAMP and that search and examination of the entire application, or in the alternative, Groups I and II, and Groups III and IV can be made without undue burden on the Examiner. This is not found persuasive because the non-elected subject matter is drawn to separate classes of invention with different classifications requiring different non-coextensive searches, as reflected in their separate classifications, which are predicated on their having a separate status in the art. The separate, non-coextensive searches constitute an undue burden necessitating separate examination and search. The response fails to adequately substantiate why the alleged related art would by necessity constitute a co-extensive search and examination.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 18-28 and 30-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention; claim 9 is provisionally withdrawn as being drawn to a nonelected species there being no allowable generic or linking claim. Applicant

timely traversed the restriction (election) requirement in Paper No. 10. Claims 7, 8, 10-17, and 29 are under examination in the instant application.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

There is not adequate support in provisional application 60/127,452 (filed 4/01/99) for the nucleic acid of SEQ ID NO:13, the amino acid sequence of SEQ ID NO:14, or for methods or compositions comprising nucleic acids encoding the mutant PAMP proteins recited in claim 14.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8, 10-17, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 10-17 are indefinite because they depend from non-elected claims (i.e. cl. 1 and 4). For purposes of examination the claims will be interpreted as being drawn to nucleic acids encoding a PAMP, or a functional fragment thereof.

Claims 7, 12, 13, 17, and 29 (and dependent claims) are indefinite in their recitation of the terms "PAMP" or "mutant PAMP", since it is unclear how these terms are defined or what their metes and bounds are so as to distinguish a PAMP-encoding nucleic acid from non-PAMP-encoding nucleic acids. The specification states that "PAMP" refers to "functionally active fragments of the protein" (p. 10, lines 11-26), which includes peptides that contain a PAMP epitope. However, the prior art teaches that an immunogenic portion is about 5 amino acids in length; thus any given amino acid sequence comprising at least 5 identical PAMP amino acids would appear to anticipate the claimed subject matter (see p. 293, part D In Levinson et al., Medical Microbiology & Immunology, third edition, 1994).

Claim 10 (and dependent claims) is indefinite in its recitation of the phrase "which is human (SEQ ID NO:13)" since it is unclear whether the scope of the claim is directed to a nucleic acid encoding a human PAMP or to a specific species of human PAMP specified by SEQ ID NO:13. If it broadly embraces human PAMP-encoding nucleic acids other than SEQ ID NO:13, it is unclear whether the term is limited to naturally occurring human PAMP-encoding species or

whether it embraces synthetic nucleic acids derived from naturally-occurring PAMP-encoding nucleic acids.

Claims 11 and 16 (and dependent claims 12 and 17) are indefinite in their recitation of the phrase "cell transfected with the vector of ..." since it is unclear whether the phrase embraces an isolated cell and/or a cell transfected in vivo. Amending the claim to --An isolated cell transfected with...-- would obviate the rejection.

Claim 14 is indefinite in its recitation of the limitations "D336, Y337, C230, and both D336 and Y337" since the claim provides no sequence context or specific SEQ ID NOs so as to define the nature of the these mutations. Further, when read in light of the specification, it is not clear how these terms relate back to the phrase "wherein the mutation results in a change to an amino acid residue selected from the group consisting of ..." since the numbered amino acids appear to be directed to the *wild type* amino acid residues of SEQ ID NO:14 rather than mutant residues.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 8, 10-17, and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to methods or compositions comprising nucleic acids "encoding the PAMP of claim 1" or to various nucleic acids encoding a "mutant PAMP of claim 4". An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its relationship to a newly identified protein-encoding region, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any other related DNA with a similar biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNAs that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC,

1997)). Adequate description of the methods first requires an adequate description of the materials, i.e. specific DNA sequences, which provide the means for practicing the invention.

Claims 7, 8, 10-17, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids comprising a PAMP-encoding nucleic acid of SEQ ID NO:13 or nucleic acids encoding the amino acid sequence of SEQ ID NO:14, does not reasonably provide enablement for any and all PAMP functional fragments or mutant PAMP-encoding nucleic acids . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that "PAMP" refers to "functionally active fragments of the protein", which includes peptides that contain a PAMP epitope or "a conserved domain relative to the *D. melanogaster* and *C. elegans* orthologues" (p. 10, lines 11-26). However, the prior art teaches that an immunogenic portion is about 5 amino acids in length; thus any given amino acid sequence comprising at least 5 identical PAMP amino acids would appear to anticipate the claimed subject matter (see p. 293, part D In Levinson et al., Medical Microbiology & Immunology, third edition, 1994). Given the relatively uncharacterized nature of this protein and the broad scope of subject matter embraced by the above definition, the specification fails to provide adequate guidance for making and using PAMP- or mutant PAMP-encoding nucleic acids commensurate with the broad scope of the claims subject matter. Further, the specification fails

to provide adequate guidance teaching how to use isolated conserved domains of PAMP commensurate with the above definition, particularly since it fails to provide adequate guidance concerning their structure/function relationships. The conserved domains represent nothing more than a starting point for experimentation.

The specification discloses various mutant PAMPs with mutations arbitrarily engineered into several of the different conserved domains identified by inspection of homology alignments (p. 43-46, Example 2). These mutants were used to study changes in $A\beta_{42}/A\beta_{40}$ ratios reflecting changes in γ-secretase mediated Aβ secretion profiles. However, apart from experimentation on the claimed invention, the specification does not provide sufficient guidance teaching how to construct and use these or other mutants, particularly since it fails to provide sufficient guidance concerning the particular functional domains critical to PAMP function or with an established nexus to Alzheimer's disease. Given the unclear significance of PAMPs to e.g. Alzheimer's disease, such mutants appear to represent nothing more than research tools in search of a use.

In addition, the term "mutant PAMP" broadly embraces virtually any nucleotide sequence encoding a PAMP that is different from wild-type. In the absence of any functional limitation tied to the mutant, however, recitation of the term "mutant PAMP" is simply a wish to identify or claim any nucleic acids encoding unspecified PAMP variants which may or may not have desirable or useful function. Without further guidance, the specification fails to provide a sufficiently enabling disclosure for making and using any and all PAMP functional fragments or mutant PAMPs commensurate with the scope of the claimed subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 10, 11, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession Number D87442, published 7/10/97).

Genbank Accession Number D87442 discloses a nucleic acid encoding a functional fragment of a presenilin associated membrane protein (PAMP) whose nucleic acid sequence is 99.9% identical to positions 145-2949 of SEQ ID NO:13, differing from the nucleic acid encoding a PAMP of SEQ ID NO:13 only insofar as missing the first two nucleotides of the initiation codon (i.e. AT) and containing two degenerate nucleotide positions corresponding to nucleotides 2274 and 2281 of SEQ ID NO:13. Given that the first methionine of the putative signal peptide sequence of the encoded PAMP protein is not present the PAMP product present in the membrane (the signal sequence is cleaved away from the processed membrane form), the nucleic acid sequence of Genbank Accession Number D87442 reads on an isolated nucleic acid encoding a functional PAMP fragment. Further, since the prior art sequence is not 100% identical (lacks first methionine) to SEQ ID NO:13, it would be broadly interpreted as reading on a mutant PAMP. In addition, the disclosed sequence inherently comprises selectable markers operatively linked to expression control sequences which can be broadly interpreted as being operatively

associated with the PAMP-encoding nucleic acid. Amending the claims so as not depend from a base claim reciting the "functional fragment thereof" language and to depend from a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:13 or a nucleic acid encoding the amino acid sequence of SEQ ID NO:14 would obviate the rejection in part. Further amending the claim to substitute "operatively associated with..." to --wherein the nucleic acid encoding the PAMP protein is operatively linked to an expression control sequence".

The nucleotide sequence of SEQ ID NO:13 and the amino acid sequence of SEQ ID NO:14 appear to be free of the art. Thus, methods or nucleotide sequences depending from this sequence would be allowable if amended to obviate the other rejections.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

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Art Unit 1632

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